Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A compound according to the general Formula (I)

the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof and the *N*-oxide form thereof, wherein:

X is CH_2 , $N-R^7$, S or O;

R⁷ is selected from the group of hydrogen, alkyl, Ar, Ar-alkyl, alkylcarbonyl, alkyloxycarbonyl and mono- and di(alkyl)aminocarbonyl;

R¹ and R² are each selected from the group of hydrogen, halo, hydroxy, $-OSO_2H, -OSO_2CH_3, alkyloxy, alkyloxyalkyloxy,\\ alkyloxyalkyloxyalkyloxy, tetrahydrofuranyloxy, alkylcarbonyloxy,\\ alkyloxyalkylcarbonyloxy, pyridinylcarbonyloxy,\\ alkylcarbonyloxyalkyloxy, alkyloxycarbonyloxy, alkenyloxy, alkenyloxy, alkenyloxy, mono- or di(alkyl)aminoalkyloxy, <math>-N-R^{10}R^{11}$, alkylthio, Alk[[,Ar]] and Het,

with the proviso that at least one of R^1 and R^2 is selected from the group consisting of Alk[[, Ar]] and Het, wherein

Alk is cyano, CN-OH, CN-oxyalkyl, alkyl, alkyloxyalkyl, alkyloxyalkyl, alkyloxyalkyloxyalkyl, alkylcarbonylalkyl, alkylcarbonyloxyalkyl, alkyloxycarbonylalkyl,

Ar-alkyl, Ar-carbonylalkyl, Ar-oxyalkyl, mono- or di(alkyl)aminoalkyl, mono- or di(alkylcarbonyl)aminoalkyl, mono- or di(alkyl)aminocarbonylalkyl, Het-alkyl, formyl, alkylcarbonyl, alkyloxycarbonyl, alkyloxyalkylcarbonyl, mono- or di(alkyl)aminocarbonyl, Ar-carbonyl and Ar-oxycarbonyl;

Ar is phenyl or naphthyl, optionally substituted with one or more halo, cyano, oxo, hydroxy, alkyl, formyl, alkyloxy or amino radicals.

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

Het is a heterocyclic radical selected from the group consisting of Het¹, Het² and Het³;

Het¹ is an aliphatic monocyclic heterocyclic radical selected from the group consisting of pyrrolidinyl, dioxolyl, imidazolidinyl, pyrrazolidinyl, piperidinyl, dioxyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl and tetrahydrofuryl;

Het² is a semi-aromatic monocyclic heterocyclic radical selected from the group consisting of 2H-pyrrolyl, pyrrolinyl, imidazolinyl and pyrrazolinyl;

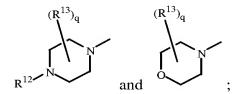
Het³ is an aromatic monocyclic heterocyclic radical selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, furyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl and triazinyl; or an aromatic bicyclic heterocyclic radical selected from the group consisting of quinolinyl, quinoxalinyl, indolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothienyl;

wherein each Het¹, Het² and Het³-radical may optionally be substituted on either a carbon or heteroatom with halo, hydroxy, alkyloxy, alkyl, Ar, Aralkyl, formyl, alkylcarbonyl or pyridinyl;

R¹⁰ and R¹¹ are each, independently from each other, selected from the group consisting of hydrogen, alkyl, Ar, Ar-alkyl, pyrrolidinylalkyl, piperidinylalkyl, piperidinylalkyl, piperazinylalkyl, morpholinylalkyl, mono- or di(alkyl)aminoalkyl, alkylcarbonyl, alkenylcarbonyl, Ar-carbonyl, pyridinylcarbonyl, alkyloxycarbonyl, mono- or di(alkyl)aminocarbonyl, mono- or di(alkyl)aminocarbonyl, mono- or di(alkyloxycarbonylalkyl)aminocarbonyl, pyrrolidinylcarbonyl, aminoiminomethyl, alkylaminoiminomethyl, N-benzylpiperazinyliminomethyl, alkylsulphonyl and Ar-sulphonyl; or R¹⁰ and R¹¹ may be taken together and with the N may form a monovalent radical selected from the group of

 $(R^{13})_q$ $(R^{13})_q$

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007



wherein:

R¹² is selected from the group consisting of hydrogen, alkyl, Ar, Ar-alkyl, Ar-alkenyl, alkylcarbonyl, alkyloxycarbonyl, alkyloxyalkylcarbonyl and monoor di(alkyl)aminocarbonyl;

each ring being optionally substituted with q radicals R¹³, each radical independently from each other selected from the group of alkyl, oxo, Ar, Aralkyl, Ar-alkenyl and alkyloxycarbonyl and q being an integer ranging from 0 to 6; or

 R^1 and R^2 may be taken together to form a bivalent radical - R^1 - R^2 - selected from

the group consisting of -CH₂-CH₂-CH₂-CH₂-, -CH=CH-CH₂-CH₂-,

-CH2-CH2-CH=CH-, -CH2-CH=CH-CH2- and

-CH=CH-CH=CH;

a and b are asymmetric centers;

(CH₂)_m is a straight hydrocarbon chain of m carbon atoms, m being an integer

ranging from 1 to 4;

Pir is a radical according to any one of Formula (IIa), (IIb) or (IIc)

$$(R^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(C)$$

optionally substituted with n radicals R⁸, wherein:

each R⁸ is independently from each other, selected from the group of hydroxy, amino, nitro, cyano, halo and alkyl;

n is an integer ranging from 0 to 5;

R⁹ is selected from the group consisting of hydrogen, alkyl and formyl; R³ represents an optionally substituted aromatic homocyclic or heterocyclic ring

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

system together with an optionally substituted and partially or completely hydrogenated hydrocarbon chain of 1 to 6 atoms long with which said ring system is attached to the Pir radical and of which may contain one or more heteroatoms selected from the group of O, N and S;

alkyl represents a straight or branched saturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic saturated hydrocarbon radical having from 3 to 6 carbon atoms, optionally substituted with one or more halo, cyano, oxo, hydroxy, formyl or amino radicals;

alkenyl represents a straight or branched unsatured hydrocarbon radical having one or more double bonds, optionally substituted with one or more halo, cyano, oxo, hydroxy, formyl or amino radicals; and halo is fluoro, chloro, bromo and iodo.

2 (Currently Amended) <u>The [[A]]</u> compound according to claim 1, <u>wherein</u> eharacterized in that R³ is a radical according to any one of Formula (IIIa), (IIIb) or (IIIc)

wherein:

- d is a single bond while Z is a bivalent radical selected from the group consisting of $-CH_2$ -, -C(=O)-, -CH(OH)-, -C(=N-OH)-, -CH(alkyl)-, -O-, -S-, -S(=O)-, -NH- and -SH-; or d is a double bond while Z is a trivalent radical of formula =CH- or =C(alkyl)-;
- A is a 5- or 6-membered aromatic homocyclic or heterocyclic ring, selected from the group consisting of phenyl, pyranyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, thienyl, isothiazolyl, pyrrolyl, imidazolyl, pyrazolyl, furanyl, oxadiazolyl and isoxazolyl;

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

p is an integer ranging from 0 to 6;

\mathbb{R}^4 is alkyl;

R⁴ and R⁵ are each, independently from each other, is selected from the group consisting of hydrogen, alkyl, Ar, biphenyl, halo and cyano; or

 R^4 and R^5 — may be taken together to form a bivalent radical - R^4 - R^5 - selected from the group consisting of -CH $_2$ -, -CH $_2$ -, -CH $_2$ -CH $_2$ -, -CH=CH-, -O-, -NH-, =N-, -S-, -CH $_2$ N(-alkyl)-, -N(-alkyl)CH $_2$ -, -CH $_2$ NH-, -NHCH $_2$ -, -CH=N-, -N=CH-, -CH $_2$ O- and -OCH $_2$ -;

each R⁶ is independently from each other, selected from the group consisting of hydroxy, amino, nitro, cyano, halo, carboxyl, alkyl, Ar, alkyloxy, Aroxy, alkylcarbonyloxy, alkyloxycarbonyl, alkylthio, mono- and di(alkyl)amino, alkylcarbonylamino, mono- and di(alkyl)aminocarbonyloxy, mono- and di(alkyl)aminoalkyloxy; or

two vicinal radicals R^6 may be taken together to form a bivalent radical $-R^6$ - R^6 -selected from the group consisting of $-CH_2$ - CH_2 -O-, -O- CH_2 - CH_2 -, $-CH_2$ -, $-CH_2$ -, $-CH_2$ -, $-CH_2$ -, and $-CH_2$ -, and an $-CH_2$ -, an $-CH_2$ -, and an $-CH_2$ -, and an $-CH_2$ -, and an $-CH_2$ -, an $-CH_2$ -, and an $-CH_2$ -, and an $-CH_2$ -, and an $-CH_2$ -, an $-CH_2$ -, and an $-CH_2$ -, and an $-CH_2$ -, and an $-CH_2$ -, an

- 3. (Currently Amended) The [[A]] compound according to claim 2, wherein X=O; m = 1; Pir is a radical according to Formula (IIa) wherein n =0; R³ is a radical according to Formula (IIIb) wherein d is a double bond while Z is a trivalent radical of formula =CH-, A is a phenyl ring, R⁴ is hydrogen or alkyl, R⁵ and R¹⁶ are each hydrogen, R⁶ is hydrogen or halo and p = 1.
- 4. (Currently Amended) The [[A]] compound according to claim 1 wherein at least one of R¹ and R² is selected from the group consisting of cyano optionally substituted with hydroxy or alkyloxy; alkyl; hydroxyalkyl; aminoalkyl; alkyloxyalkyl; alkyloxyalkyl; alkyloxyalkyl; ar-oxyalkyl; mono- or di(alkyl)aminoalkyl, the alkyl radicals optionally substituted with hydroxy; mono- or di(alkylcarbonyl)aminoalkyl; mono- or di(alkyl)aminocarbonyl; piperidinylalkyl; morpholinylalkyl; phenyl and thienyl optionally substituted with alkylcarbonyl.

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

5. (Currently Amended) The [[A]] compound according to claim 1 selected from the group consisting of:

- 8 Methyl 3 [4 (3 phenyl allyl) piperazin 1 ylmethyl] 3a,4 dihydro 3H chromeno[4,3 c]isoxazole;
- 8-Methoxy-7-methyl-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole;
- {8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazol-7-yl}-methanol;
- 7-Methoxymethyl-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazole;
- 8-Methoxy-7-(2-methoxymethoxymethyl)-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole;
- Acetic acid 8-methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazol-7-ylmethyl ester;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-7-phenoxymethyl-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole;
- 2-(Methyl-{3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazol-7-ylmethyl}-amino)-ethanol;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-7-morpholin-4-ylmethyl-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole;
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbaldehyde oxime;
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbaldehyde O-methyl-oxime;
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbonitrile;
- N-{3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3H-chromeno[4,3-c]isoxazol-7-ylmethyl}-acetamide;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazole-7-carboxylic acid ethylamide;
- 8 Methoxy 3 [4 (2 methyl 3 phenyl allyl) piperazin 1 ylmethyl] 7 phenyl 3a,4 dihydro 3H chromeno[4,3 c]isoxazole; and
- 1-(5-{8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

dihydro-3*H*-chromeno[4,3-c]isoxazol-7-yl}-thiophen-2-yl)-ethanone.

6. (Original) A compound which is degraded *in vivo* to yield a compound according to claim 1.

- 7. (Canceled)
- 8. (Withdrawn/Currently Amended) A method for the treatment and/or prophylaxis of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders comprising administering a therapeutically effective amount of [[the]] a compound [[of]] according to claim 1.
- 9. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient a therapeutically effective amount of a compound according to claim 1.
- 10. (Withdrawn/Previously Presented) A process for making a pharmaceutical composition comprising mixing a compound according to claim 1 and a pharmaceutically acceptable carrier.
- 11. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient a therapeutically effective amount of a compound according to claim 1 and one or more other compounds selected from the group consisting of antidepressants, anxiolytics and antipsychotics and anti-Parkinson's disease drugs.
- 12. (Canceled).
- 13. (Withdrawn/Currently Amended) A method for the treatment and/or prophylaxis of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders, said treatment comprising the simultaneous or sequential administration of a therapeutically effective amount of a compound according to

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

claim 1 and one or more other compounds selected from the group consisting of antidepressants, anxiolytics, anti-psychosis and anti-Parkinson's drugs.

- 14. (Withdrawn/Currently Amended) The method of claim 13 wherein the treatment and/or prophylaxis is for depression, anxiety and body weight disorders, said treatment comprising the simultaneous or sequential administration of one or more compounds selected from the group consisting of antidepressants, anxiolytics and antipsychotics and anti-Parkinson's disease drugs and a compound according claim 1.
- 15. (Withdrawn/Previously Presented) A process for making a pharmaceutical composition to improve efficacy and/or onset of action in the treatment and/or prophylaxis of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders comprising mixing a pharmaceutical excipient, a therapeutically effective amount of one or more compounds selected from the group consisting of antidepressants, anxiolytics and antipsychotics and anti-Parkinson's disease drugs and a compound according to claim 1.
- 16. (Withdrawn/Previously Presented) A process for making a pharmaceutical composition comprising mixing a compound according to claim 1 and a compound selected from the group consisting of antidepressants, anxiolytics, antipsychotics and anti-Parkinson's disease drugs and a pharmaceutically acceptable carrier.